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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/245,615	02/04/99	HOEFFLER J	INVIT1100-1

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1641	10

DATE MAILED: 10/25/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/245,615	Hoeffler et al.
Examiner	**Group Art Unit**
Lisa V. Cook	1641

☒ Responsive to communication(s) filed on *Jul 26, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-59* is/are pending in the applicat

Of the above, claim(s) *1-30 and 41-50* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *31-40 and 51-59* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-59* are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892 ✓

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4,5,6,&8* ✓ ✓ ✓ ✓

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948 ✓

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Preliminary Amendment

1. In response to Applicant's Amendment-A, filed 7/26/00 (paper #9) -claims 31 & 37 have been amended and new claims 51-59 have been added. The amendment and new claims were presented to define the invention with greater particularity. (See page 4, 1st paragraph).

Election/Restrictions

2. Applicants' provisional election with traverse of Group IV (claims 31-40 and 51-59) in Paper #9, filed 7/26/00 is acknowledged. Applicant argues that the claims were inappropriately divided because all of the claims in Groups I-IV have a "common requirement" – namely an array of a plurality of antibodies located at discrete locations on a solid surface pertaining to biological molecules. Therefore, applicant states that a search for any of the claims in Groups I-V would necessarily entail the search for all of the groups.

This is not found persuasive because MPEP § 808.02 recites:

> Where related inventions as claimed are shown to be distinct under the criteria of MPEP § 806.05(c)- § 806.05(i), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof, (B) A separate status in the art when they are classified together, or (C) A different field of search.

In the instant case, (A) -The Restriction Requirement under 35 U.S.C. § 121 in Paper #7 is still deemed appropriate, establishing distinctness of the inventions and separate classification thereof:

(B) The inventions of Groups I, II, III, IV, and V would require a separate status in the art when they are classified together; the invention as a whole is drawn to antibody detection via antigen binding. Such inventions are classified in 435, subclass 7 for example.

(C) With respect to a different field of search – Because these inventions are distinct and have acquired separate status in the art as shown by their different classification, recognized divergent subject matter and because the search required for each invention is not substantially coextensive with the search required for the remaining invention, restriction for examination purposes as indicated is proper. Please note that the classifications in the restriction are illustrative only and do **not** represent all the classes and subclasses which must be searched for each invention; nor is the search limited to issued US patents, but rather includes published foreign patents and applications as well as literature search.

3. Further, the combination of Groups I, II, III, IV, and V for examination on the merits is deemed incorrect. The merging of these groups would combine patentably distinct inventions: (Group I – Claims 1-17 and 25 comprise a method of identifying an antigen; Group II – Claims 18-24, 26, 27, and 48-50 are directed to methods of comparing protein expression in a cell – which encompasses more complex procedures beyond mere antibody identification; such as isolation, purification, product integrity, and stability; Group III - Claims 28-30 are directed to a method of diagnosing a disorder, while Group V – Claims 41-47 compare protein expression by specifically utilizing nucleic acid probes. The kits found in Group IV are also distinct because they can be employed in any of the previously mentioned materially different processes of Groups I, II, III, or V. (Applicant confers in paper#9, page 4, last paragraph). Although the methods have a "common requirement" they are unrelated because they are not disclosed as capable of use together and they have different modes of operation, different functions, and detect different effects. For these reasons the inventions of Groups I, II, III, IV, and V were not joined.

Remarks

4. Examiner erroneously did not include claim 27 in the restriction requirement set forth in Paper #7, mailed 6/20/00. The claim should be included in the invention of Group II drawn to protein expression. The clarification of grouping has been stated in this action to eliminate any ambiguity and because the instant claim is withdrawn as to a non-elected invention this does not have any merits with respect to the instant action.

The Restriction Requirement is still deemed proper and is therefore made **FINAL.**

5. Currently, claims 1-59 are subject to Restriction and Election Requirement. Claims 1-30 and 41-47 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as claims drawn to a non-elected invention. Claims 31-40 and 51-59 are pending and under consideration.

Priority

6. If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed copending application, specific reference to the earlier filed application (60/073,605-filed 2/4/98) must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Drawings

7. The drawings in this application are objected to by the Draftsperson under 37 CFR 1.84 or 1.152 (see PTO-948). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Information Disclosure Statement

8. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449 have cited the references they have not been considered.

9. The information disclosure statement filed 11/1/99 - Paper#3, fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each document listed that is not in the English language. The reference – Hepato-Nephromegalia Glykogenica, E.Von Gierke, p.498-513 was not considered because it did not include a certified English translation of the full document or a concise explanation of relevance. It has been placed in the application file, but the information referred to therein has not been considered.

Specification

10. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The use of the trademark "Startalinker" has been noted in this application. (See page 37, line12- for example). It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 31-40 and 51-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 52 and 56 are vague and indefinite because it is unclear as to what the term "spatially addressable" entails. The claim recites antibody arrangement, but the term is not defined in the disclosure. Without clear definition of the term the metes and bounds of the claim can not be determined. Please define applicants intended meaning to obviate this rejection.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 31-32, 36-38, and 51-59 are rejected under #35 U.S.C. 102(b) as being anticipated by Vestal (U.S.Patent#5,498,545).

Vestal teaches a system for analyzing samples. The system entails a sample holder comprising a surface upon which a plurality of biological samples are placed and measured for mass quantification.

The samples may alternatively be placed on the ends of removable pins (applicants discrete locations) and the pins locked into a two dimensional array using a sample holder (applicants solid surface) positioned on a plate. Samples of interest can be deposited in know locations on the spots on the surface of the sample holder. Alternatively, the system may be used to deposit samples by blotting from a two-dimensional gel, in this case the samples are distributed in an unknown pattern over the sample surface (Column 5, Lines 1-6).

Samples undergo a reaction, for example DNA sequencing and are allowed to dry (Column 5, Lines 52-60). The plate is transferred to a vacuum chamber. This system is suitable for loading the samples into the mass spectrometer without venting the mass spectrometer vacuum system (Column 8, Lines 29-34). The sample plate is then transported to the ion source.

The system allows for any selected point on the sample plate to be positioned precisely (within one thousandth of an inch) on the axis of the mass spectrometer. The sample is irradiated by the laser beam, ions may be produced from each sample plate and the plate is automatically rotated between sample positions with respect to the laser beam (Column 10, Lines 3-12).

The mass spectrum is obtained by calculating the centroid and integral intensity of each peak. The mass determination also takes into account peaks that are known to be due to matrix and other extraneous material. Thereby providing a more accurate mass determination. (Column 11 and 12). The reference inherently encompasses applicant kit and kit instructions.

II. Claims 31-32, 36-38, and 51-59 are rejected under #35 U.S.C. 102(b) as being anticipated by Heller et al. (U.S.Patent#5,605,662).

Heller et al. disclose a microelectronic device designed and fabricated to carry out molecular biological reactions in a microscopic format. In one embodiment addressable micro-locations (applicants discrete locations) are positioned on a substrate (applicants solid surface). See for example, figures 8[a-d] and 9[a-c]. The reactions include molecular biological procedures, such as nucleic acid hybridization, antibody/antigen reaction, and related clinical diagnostics. In addition the device is employed in biopolymer synthesis. In general the device has large micro-locations (>100 microns) and can be fabricated in three dimensional formats (e.g. tubes or cylinders) in order to carry a large amount of the binding entities. The device is has utility in a variety of materials, including plastic, rubber, silicon, glass or ceramics (Column 14, Lines 25-41).

A specific example of a 96 microlocation device is illustrated in Fig. 5 of this invention. The micro-location device is fabricated from a suitable material stock and 96 proportionately spaced holes are drilled through the material. An electrode circuit board is formed on a thin sheet of plastic, which fits precisely over the top of the micro-location component. The underside of the circuit board contains the individual wires to each micro-location. Each micro-location has an individual buffer reservoir which separates adjacent surfaces. The wiring is coated with a suitable water-proof insulating material. The device is partially immersed and operates in a common buffer reservoir, applicants interconnected sumps for drainage. (Column 14, Lines 41-60). The reference inherently encompasses applicant kit and kit instructions.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 33, 34, 35, 39, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vestal (U.S.Patent#5,498,545) or Heller et al. (U.S. Patent #5,605,662) in view of Patterson et al. (U.S. Patent#5,821,063).

Please see previous discussion of Vestal (U.S.Patent#5,498,545) and Heller et al. (U.S.Patent#5,605,662) as set forth above.

Vestal and Heller et al. differs from the instant invention in not teaching single chain/stranded or recombinant antibody compositions.

However, Patterson et al. disclose methods and apparatus useful for sequencing polymers using mass spectrophotometry. The invention involves a novel sample holder for mass spectrometers. The sample holder has a reaction surface with spatially separated areas having differing ratios of polymer and hydrolyzing agent. The reaction surface can be fabricated from a variety of substrates, such as metals, foils, plastics, ceramics, and waxes. The surface can assume any configuration including a genetic probe. After incubation, a plurality of areas containing the hydrolyzed polymer fragments are ionized in a mass spectrometer. The data represents the mass to charge ratio of the fragment (Column 3, Lines 1-11). The method is deemed suitable to any hydrolyzing agent capable of hydrolyzing a polymer. Further, the polymer could be hydrolyzed

with combinations of agents including enzymatic and non-enzymatic hydrolyzing agents (Column 3, Lines 53-60).

The polymer is taught to be a naturally-occurring or synthetic moiety. It is a biopolymer selected from, but not limited to the following group: proteins, peptides, DNAs, RNAs, PNAs, carbohydrates, and modified versions thereof (Column 6, Lines 9-14). Patterson et al. disclose utility in genetic probes, which encompass the instant inventions ss(single strand) and/or recombinant antibodies.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use recombinant single stranded antibodies as taught by Patterson et al. in the method of Vestal or Heller et al. to perform multiple sample analysis/sequencing in the rapid detection kits systems because such recombinant single chain antibody combinations as taught by Patterson et al. are well known in the art. A person of ordinary skill in the art would have had a reasonable expectation of success utilizing such a compounds because Patterson et al. disclosed that his methods and compounds produced faster sequence results by eliminating preliminary optimization steps, which are tedious and time consuming. Further, the method is taught to consume less reagents and is more accurate by interpreting data from a plurality of parallel mass spectra sample readings (Column 2, Lines 41-67).

14. For reasons aforementioned, no claims are allowed.

Remarks

15. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

Levis et al. (U.S. Patent#5,580,733) disclose method for determining the nucleotide sequence of a polynucleotide by using mass spectrometry to determine the molecular weights of individual single stranded nucleic acid molecules in a population including a plurality of single-stranded nucleic acid molecules.

Vestal et al. (U.S. Patent#5,627,369) teach a time-of-flight mass spectrometer for measuring the mass-to-charge ratio of a sample molecule. The spectrometer has an independent control of the electric field experienced by the sample before and during the ion extraction.

Zuk et al. (U.S. Patent#4,281,061) teach that "as a matter of convenience the reagents [of an immunoassay] can be provided as kits, where the reagents are in predetermined ratios, so as to substantially optimize the sensitivity of the assay in the range of interest" (column 22, lines 63-66).

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook

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CM1-7D16
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10/23/00

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